

**REMARKS**

This is in response to the Action mailed September 12, 2006.

Claims 1-12 have been amended in order to recite positive method steps and to make them more consistent with U.S. practice. No change in claim scope is intended or believed made. Claim 14 has been amended to specify that R<sup>2</sup> comprises a tri-substituted phenyl radical, and new claims 17-18 further specify the R<sup>2</sup> radical. Support for the amendment is in the specification at, e.g., page 12, lines 21-26.

**35 USC §§112 and 101**

Reconsideration and withdrawal of the rejections of claims 1-12 under 35 USC §§112, second paragraph, and 101 are respectfully requested. It is believed that the present amendments to claims 1-13 have overcome these rejections.

**35 USC §103**

Reconsideration and withdrawal of the rejection of claims 1-16 under 35 USC §103 as being unpatentable over the combination of WO 92/08709 and WO 00/17158 are respectfully requested.

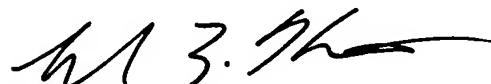
With respect to claims 1-13, those claims recite methods for the treatment or prevention of urokinase-associated or urokinase receptor-associated diseases via the administration of certain 3-guanidino phenylalanine derivatives. As the Action acknowledges, the compounds of WO '709 are taught to prevent blood coagulation or thrombosis, and there is apparently no teaching or suggestion in WO '709 that the compounds would be useful for the presently claimed purposes. The Action relies on WO '158 as allegedly providing that suggestion, but it is respectfully submitted the one of ordinary skill would not be so led by that reference.

The compounds disclosed in WO '158 are quite different from the compounds recited in present claims 1-13. The WO '158 compounds are all amidino compounds (*i.e.*, they all have the C(NH)(NH<sub>2</sub>) substituent on the phenyl ring), whereas the presently claimed compounds are all guanidino compounds having the NH-C(NH)NH<sub>2</sub> substituent on the phenyl ring. Even with WO '158 in hand, one of ordinary skill would not be led to substitute a guanidino group for an amidino group. There is no suggestion from the references that one would expect guanidino compounds to be urokinase inhibitors from the mere fact that amidino compounds are urokinase inhibitors, and both amidino and guanidino compounds inhibit thrombosis. WO '158 suggests many variables in other portions of the molecule, but all of the compounds contain the amidino group, with no suggestion of variation at that point. It is respectfully submitted that it is only in hindsight with the benefit of the present applicant's specification can it be said to be obvious to modify the WO '158 compounds as posited. Moreover, even if there were motivation in the art to make that change, one would still not have the necessary expectation of success after the modification was made. The references relied on do not provide any structure/activity link between amidino and guanidine groups in the context of inhibiting urokinase activity. Thus, the rejection should not be maintained.

The rejection is also defective with respect to claims 14-16. Those claims all recite that R<sup>2</sup> comprises a tri-substituted phenyl radical, preferably a 2,4,6-substituted phenyl radical. In contrast, the WO '709 guanidino compounds at R<sup>4</sup> apparently do not disclose or suggest those radicals.

It is believed that the present case is in condition for allowance, and a favorable Action is respectfully requested.

Respectfully submitted,



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